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EXAMINER	
ALLEN, M	

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DATE MAILED: 06/24/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

IDS 2/22/96 and 3/19/96

☒ This application has been examined ☒ Responsive to communication filed on 3/19/96 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449. 2 pages
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 38-54 and 57-69 are pending in the application.
   Of the above, claims 38-54 are withdrawn from consideration.
2. ☒ Claims 1-37, 55-56, 70 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 57-69 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Claim 70 has been cancelled. Claims 38-54 have been withdrawn as being directed to a non-elected invention. Claims 57-69 are under consideration by the Examiner.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's arguments filed 19 March 1996 have been fully considered but they are not deemed to be persuasive.

The oath or declaration remains defective because non-initialed alterations have been made to the oath or declaration (see 37 C.F.R. §§ 1.52(c) and 1.57). It is noted that applicant's response indicates that a substitute declaration will be submitted.

Claims 57-61 and 64-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7-15, and 17-18 of copending application Serial No. 08/465,652.

Claims 64-69 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 and 29-35 of copending application Serial No. 08/125,038.

Claim 64-69 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of 07/988,194 (U.S. Patent No. 5,359,046).

Specifically, the claims in the instant application and each application named above encompass overlapping embodiments of chimeric proteins and the DNA sequences that encode them or these DNA sequences contained in a cell, although claimed with different scope and differing language.

These are *provisional* obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d

887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the specification, as originally filed, does not provide support for the invention as is now claimed.

Claim 60 has been amended to recite "wherein said heavy chain of immunoglobulin is by itself or in a protein complex with a light chain." No basis has been pointed to in the application for such a limitation and none is apparent. Contrary to applicant's assertion, the examiner did not suggest any claim language.

Claims 60-61 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claim 61 is rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim 60 does not include single-chain antibodies. As such, claim 61 does not possess the limitations of the independent claim.

Claims 57-69 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited

to chimeric proteins as set forth in the prior Office action. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Applicant's arguments with respect to unspecified messenger systems are not persuasive. Reference to page 2, lines 5-11, does not remedy this deficiency. The phenomena described here (e.g. autophosphorylation) are not disclosed as messenger systems and do not define the metes and bounds of what was intended by the phrase "messenger system." Specific second messenger systems are described at page 2, lines 12-14. If applicant intended to include such phenomena as autophosphorylation as well as second messenger systems in the claims, the claims should recite specifically what was intended. Contrary to applicant's assertion, there is no evidence that the phrase "messenger system" would denote more than known second messenger systems to one of ordinary skill in the art. Applicant is cautioned against introducing new matter.

Applicant argues that the models of Stoddard et al. do not apply to the instant invention. Stoddard et al. (Cold Spring Harb. Symp. Quant. Biol., 57:1-15, 1992) was cited as the most recent review article found by the Examiner discussing the mechanisms by which receptors generate transmembrane signaling to initiate intracellular events. The fact that three of the models (A, B, and C) are discussed in terms of naturally occurring receptors and applicant's claims are directed to non-naturally occurring receptors does not detract from the general principles discussed. Applicant argues that model D could also be construed as indicating that the receptors associate and then an event such as phosphorylation causes a conformational change. The summary of model D by the Examiner did not preclude such an interpretation and again does not detract from the general principles discussed. It appears that applicant is arguing that only a model with a clustering mechanism as discussed by Kolanus et al. is relevant. Applicant argues that clustering of cytoplasmic domains is necessary and sufficient to result in signalling. First of all, there is no evidence that the results of Kolanus et al. are universally applicable to all cell signalling by naturally and/or non-naturally occurring receptors. It is noted that the claims are not limited to the chimeric receptors of Kolanus et al. Secondly, the principles discussed with respect to the models of Stoddard et al. are equally applicable to this model. That is, Kolanus et al. requires that the chimeric receptor possess a three dimensional structure suitable to cluster chimeric receptors correctly to initiate an intracellular signal. The clustering of Kolanus et al. requires that the extracellular domains have a three dimensional structure suitable for an antibody to hold at least two of the receptors together to form the cluster. Even if the extracellular domains can be clustered, this does not guarantee that the cytoplasmic

domains are in the correct position to associate and generate a signal. In fact, Kolanus et al. demonstrates that the properties of chimeric receptors are unpredictable. The authors found it surprising that a chimeric receptor with a Src family kinase intracellular domain did not initiate a signal whereas one with a Syk or ZAP-70 kinase did. (See abstract and page 173, left column, first complete paragraph.) Even if the clustering mechanism was the correct and only mechanism for all cell signalling, the specification provides no guidance as to selecting from the myriad of combinations encompassed by the claims those chimeric receptors that would be expected to result in a chimeric protein having the requisite properties. It is not relevant that one could assay for various activities. Applicant has not established that one could extrapolate the results in the specification to predict the activities of chimeric receptors commensurate in scope to the claims. The specification does not provide guidance for other combinations likely to be successful. The claims are an invitation to experiment and it would require undue experimentation to practice the invention as claimed.

Applicant cites In re Borkowski et al. (CCPA 1970) 442 F2d 904, 164 USPQ 642 and In re Anderson (CCPA 1973) 471 F2d 1237, 176 USPQ 331. The instant application can be distinguished from In re Borkowski et al. in that it is not discernible from the specification or arguments what the "best mode contemplated" is. Is it using CD4? Is it using the zeta chain? Is it using a transmembrane domain from one or the other? Is it using domains from proteins known to be present in T cells and participate in antigen recognition? The instant application can be distinguished from In re Anderson in that no requirement was made for exemplification of every embodiment. The enablement rejection points out that an insufficient number have been demonstrated where a reasonable extrapolation to the rest encompassed could be made.

Applicant refers to the chimeric receptors of Letourneur et al., Eshhar et al., and Romeo et al. These receptors are not specifically suggested by the specification even though they use domains exemplified in the specification or domains similar to those exemplified in the specification. They are not commensurate in scope to support the breadth of the claims.

Applicant points out that the claims preclude using an intracellular domain from a G-protein coupled receptor because of the limitation that the cytoplasmic domain cannot be naturally joined to an extracellular ligand binding domain. Therefore, this part of the rejection in the prior Office action (page 5, second complete paragraph and the specific example given in the fourth complete paragraph) is withdrawn.

The claims have been amended to recite "mammalian host cell." Therefore the part of the rejection in the prior Office action concerning host cells (page 5, third complete paragraph) is withdrawn.

It is believed that all pertinent arguments have been addressed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen, whose telephone number is (703) 308-0666. The examiner can normally be reached on Monday-Thursday from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Garnette D. Draper, can be reached on (703) 308-4232. The most convenient FAX telephone number for Art Unit 1812 is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1800